

## REMARKS

Currently pending are Claims 1, 5-8, 10, 12-76, 80-83, and 87-139, of which Claims 14-75, and 89-136 have been withdrawn. Claim 85 has been cancelled. Claims 1, 13, 76, 88, and 137-139 have been amended.

Claims 1, 76 and 139 have been amended to use the term “weight gain and development,” which finds support in the specification where it is stated that in addition to having higher birth weights (please see specification, Examples 14, 15, and 21), the offspring of treated females had changes in hormonal profile in early development (please see paragraph 159, and Tables 6-12), changes in body composition (please see specification, paragraphs 144 and 147), and changes in other biochemical and hormonal parameters (please see specification, paragraph 152, and Tables 6 - 12). Claims 137 and 138 have been amended to remove reference to “a polypeptide”. Claim 139 has been amended as described above, as well as to include the term “electroporating an effective amount of vector”, which is supported throughout the specification, particularly in [0067], [0133], [0134], [0189], [0209]. No new matter has been added.

**The outstanding objection to claim 85 is now moot in light of Applicants having cancelled Claim 85.**

## **II. Double Patenting Rejection–Schwartz ‘693 in view of Aihara, in further view of Kann**

The Examiner has made a new rejection of Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 on the grounds of obviousness-type double patenting over Claims 21-23 of Schwartz et al (U.S. Patent No. 6,423,693, “the ‘693 Reference”) in view of Aihara et al. (“the Aihara Reference”), in further view of Kann et al. (U.S. Patent No. 5,061,690). Applicants respectfully traverse.

Although Claims 21-23 of the ‘693 Reference describe a method for transfecting cells *in vivo*, they are not directed towards methods of “improving or enhancing weight gain and

development in an offspring from a female mammal” by electroporating the female mammal prior to or during gestation of the offspring with a GHRH expressing vector (see Claim 1 as representative of claimed invention). Applicants therefore respectfully submit that the double-patenting rejection is not proper.

Applicants respectfully point to the error in the Patent Office rationale that is the basis for this rejection, which is that “while Schwartz is silent as to whether treatment of pregnant mammals with GHRH plasmid would necessarily result in offspring that exhibit increased weight gain, the offspring of treated mothers would have necessarily exhibited weight gain” (see page 6, rows 1-3 of the Office Action of 12/28/06). The art as a whole available to one of ordinary skill at the time of filing does not necessarily lead to this conclusion. For instance, one of ordinary skill would have known Lacroix et al. (Lacroix et al. *Biol Reprod.* 2002 Mar; 66(3):555-61, “the Lacroix Reference”), which shows that if GHRH is administered under certain conditions, no increases in ovine GH or prolactin (PRL) are obtained. The authors state that “Ovine placenta produces growth hormone-releasing hormone (GHRH), but addition of GHRH to the perfusion medium did not modify either oPGH or oPL production” (Please see abstract of the Lacroix Reference). This demonstrates that the introduction of GHRH does not necessarily result in changes in the levels of GH or related molecules in animal tissue. In fact, the addition of GHRH can result in similar levels of GH in an animal.

The Patent Office cites to the Aihara Reference for the suggestion that electroporation is an efficient approach for muscle-targeted gene expression, and that this suggestion in combination with the claims of the ‘693 Reference to arrive at the currently-claimed invention. However, Applicants submit that the Aihara Reference does not disclose the delivery of treatment to a subject to improve or enhance weight gain and development in an unborn offspring. The Aihara Reference describes treatment of an animal to obtain a certain effect in that same animal, rather than treating an animal to obtain an effect in the offspring.

Finally, the Patent Office cites to the Kann Reference as providing that pregnant ewes, administered hGHRH protein, gave birth to lambs that were significantly heavier than lambs from untreated mother and had greater weight gain than lambs from an untreated mother. The Patent Office attempts to combine the Kann Reference with the other two references to arrive at

the current invention. However, Applicants submit that the Kann Reference is distinct from the current application in at least two ways. First, the animals in the reference were injected twice daily from day 137 up to littering with a human GHRH analog, human GHRH(1-29)NH<sub>2</sub>. The method of the Kann Reference is directed to supplying a pregnant female mammal an effective amount of human GHRH **protein, NOT plasmid** via electroporation as in the current application. Moreover, the injection of the protein described in the Kann Reference does not result in improved or enhanced weight gain and development in the offspring as with the current invention.

In light of these arguments, Applicants respectfully submit that the current Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 are patentably distinct from the cited reference, either alone or in combination.

### **III. Double Patenting Rejection—Application No. 10/315,907**

The Examiner has rejected Claims 1, 5-8, 10, 12, 76, 80-83, 85, 87, 137-139 over Claim 1 of Application No. 10/315,907 (“the ‘907 Reference”) in view of an online publication, “the BabyCenter Reference”. Applicants respectfully traverse.

The current application describes a method for improving or enhancing weight gain and development in an offspring from a female mammal - not in the subject itself. The Patent Office states that the treatment of pregnant women for anemia with the method of Claim 1 of the ‘907 Reference would necessarily result in offspring that exhibited increased weight gain. There is nothing in the art to suggest that such combination happened or that there was a motivation to treat a pregnant, anemic mammal with a vector capable of expressing GHRH. The animals treated in the current application were not anemic, as all biochemistry and hormonal levels were within normal limits for the species prior to treatment. Further, nothing in the art suggested that one of ordinary skill would look to treat of an anemic, pregnant mammal, especially for the purposes of enhanced weight gain in the offspring.

Therefore, the ‘907 Reference, alone or in combination with the BabyCenter Reference, would not have rendered the currently-claimed invention obvious. Applicants respectfully submit that the obviousness-type double patenting rejection be withdrawn.

**IV. Double Patenting Rejection–Application No. 10/359,919**

The Examiner has rejected Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 of the current application over Claims 1-20, 23-40, 43, 47, 48, 50, 51, 55-57, 59, 62, 65, 75-77, 82 of Application No. 10/359,919 (“the ‘919 Reference”). Applicants respectfully traverse.

Applicants respectfully submit that a *prima facie* case of obviousness in view of the claims of the ‘919 Reference has not been established in this case. A person of ordinary skill in the art, who was aware of the method claimed in the ‘919 Reference, would not have had suggestion or motivation to use such a method in an attempt to improve or enhance the weight gain and development of offspring by treating the pregnant female mammal. Although one of skill in the art might have been aware that prolactin is primarily associated with lactation in a subject, prolactin has not been directly linked to weight gain and development, e.g., parameters such as body weight or composition, in the offspring of a treated female mammal.

Moreover, one of ordinary skill in the art would not have had a reasonable expectation of success with such an attempt. In the complex field of DNA transfection in vivo, at best, a great deal of experimentation would be necessary to determine the effect of this method on any given molecule.

In light of the above-arguments, Applicants respectfully submit that the claims of the current application are patentably distinct from the claims of the ‘919 Reference, either alone or in combination. Applicants request that the current rejection be withdrawn.

**V. Double Patenting Rejection–Application No. 10/764,818 in view of Kann, in further view of Aihara**

The Examiner has also rejected Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 of the current application over Claims 1-4, 7, 9, 11-20, 22, 44, 45, 48-57, 63, 69, and 75 of Application No. 10/764,818 (“the ‘818 Reference”) in view of Kann et al. (“the Kann Reference”), in further view of Aihara et al. (“the Aihara Reference”). Applicants respectfully traverse.

As described in detail in the above arguments, the current claims solve a distinct problem from the problem solved by the claims of the ‘818 Reference. Applicants respectfully submit

that there was no teaching or suggestion available to one of skill in the art that the method of the '818 Reference could be modified to result in improved growth characteristics in an offspring. Even when combining the '818 Reference with the Kann Reference and the Aihara Reference, there is insufficient teaching or suggestion to render the current claims obvious. The Kann Reference does not suggest the use of a technique which results in enhancement of weight gain and development in the offspring of a female mammal by treating the female mammle; instead, the reference describes repeated treatments. This disclosure would not have motivated one of skill in the art to seek a transfection-based method for combination with the Kann Reference. The Aihara Reference describes a method of using steel electrode needles, but there is no suggestion of using these in combination with a method such as the one claimed in the '818 Reference.

Applicants therefore respectfully submit that the cited references, alone or in combination, are not sufficient to render the currently claimed material obvious, and that the current claims are patentably distinct from the claims of the '818 Reference.

#### **VI. Rejection under USC §112-New Matter**

The Examiner has rejected Claims 137 and 138 on the grounds that they introduce new matter. In response, Applicants have amended the claims to recite remove reference to a "polypeptide." Applicants submit that this amendment renders Claims 137 and 138 to be in condition for allowance.

#### **VII. Rejection under USC §112-Enablement**

The Examiner has pointed out that, although the remarks in the Applicants' Response filed October 10, 2006, described the amendment of Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, 137-139, the amendments were not made to the claims. Applicants have now made the amendments.

Applicants wish to point out to the Examiner that the amendments were made to independent Claims 1, 76, and 139 only, and these changes address the Examiner's concerns regarding both the independent claims and the dependent claims.

**VIII. Rejection under USC §112-Enablement**

The Examiner has pointed out that Applicants have not responded to the Examiner's rejection of Claim 139 in the Office Action of June 16, 2006, on the grounds that it encompasses a method of introducing a vector to muscle cells via any route, including intravenous administration.

In response, Applicants have amended Claim 139 to recite "electroporating an effective amount of a vector..." Applicants submit that Claim 139 is now in condition for allowance.

**IX. Rejection under USC 35 §103–Schwartz et al. in view of Aihara, in further view of Kann**

The Examiner has rejected Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 of the current application as being obvious in view of the '693 Patent, in view of the Aihara Reference, and in further view of the Kann Reference.

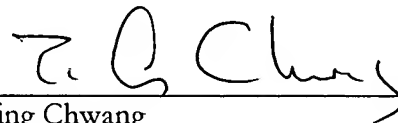
As described in detail above, the method described in the '693 Reference contains several distinct elements from the currently-claimed invention. In addition, the Aihara and Kann References do not provide additional elements which, taken in combination with the '693 Reference, would render the currently-claimed invention obvious.

Applicants submit that, on the basis of the above arguments, the cited references fail to render the current claims obvious and this rejection should be withdrawn.

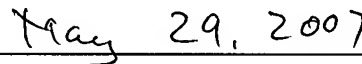
**X. CONCLUSIONS**

Applicants respectfully submit that, in light of the foregoing amendments and argument, Claims 1, 5-8, 10, 12, 13, 76, 80-83, 87, 88 and 137-139 are in condition for allowance. A Notice of Allowance is therefore requested.

Respectfully submitted,



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